IDENTITY PRESERVED PRODUCTION AND THE COMMERCIAL DEVELOPMENT OF NOVEL MEDICINAL AND COSMETIC PLANTS

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Abstract

Throughout history, plants have been a major source of pharmaceutical and cosmetic ingredients. Well known examples include the use of hemp oil in cosmetics, GLA based products as skin moisturisers and the production of poppies for the manufacture of morphine and codeine. However, for every success story there are probably a hundred failures and the commercialisation of a novel crop is not an easy, quick or cheap exercise.

To be successful the R & D focus must be market orientated. Only too often breeding programmes which are product-orientated fail to provide a suitable return on their investment and are discontinued. Despite having achieved significant improvements, either in terms of yield or agronomic qualities they fail to succeed because the market does not want, need or value the claimed advantages they offer. An understanding of the target markets' characteristics, and identifying customers who are prepared to form close partnerships, will inevitably be more successful in the long term. Only when the target active ingredient, or use, has been qualified, does the long and detailed process of evaluating nature's options to satisfy this demand begin. Conventional plant breeding, the domestication of wild plants or even genetic modification, all have a place in achieving the final goal.

Key questions have to asked throughout this evaluation process including whether the end product will have a quality that is stable, is able to be replicated and offer 100% confidence to the customer. A detailed agronomic programme has to be implemented, along with a review of the geographically most suitable production areas in order to offer both competitive and guaranteed sources of raw material.

One of the concerns often levelled against plant derived products is the lack of consistency in achieving standardised levels of active ingredients. For this reason therefore, it is essential to have an Identity Preserved production system once a variety of novel plant has been identified. Full traceability from the sowing seed through to the finished extracted product is only part of the quality assurance programme. Documented production systems, open to audit and scrutiny by the end user, can have a significant effect on the finished products' quality characteristics.

This paper presents a background to the commercialisation of novel crops as well as the importance of an Identity Preserved production system.

Key Words
Identity Preserved, Novel crops, Commercialisation, Traceability

1. Introduction

Throughout history, plants have been a major source of pharmaceutical and cosmetic products. Well known examples include the use of Hemp oil in cosmetics, GLA based products in skin moisturisers, and the production of Poppies for the manufacture of morphine and codeine. However, for every success story there are probably a hundred failures and the commercialisation of a novel crop is not an easy, quick or cheap exercise.

One of the concerns often levelled against plant derived products is the lack of consistency in achieving a standardised level of active ingredient. For this reason, it is essential to have an Identity Preserved (IP) production system once a variety of novel plant has been identified. This paper reviews the importance of IP systems, along with the commercial development of novel medicinal and cosmetic plants.

In order to provide a background to this presentation, I would like to briefly describe the company I work for, John K King & Sons Ltd, who contract grow a significant acreage of Identity Preserved Crops throughout the world. Kings core business is the development of novel crops, nearly always alongside a customer who has a very specific need to satisfy. Crops are then grown on an Identity Preserved basis with the customer being supplied with seed, oil or specific extracted active ingredient. Owned by Associated British Foods plc, Kings is based in Essex in the UK, and contract grow their crops throughout the world, but with particular emphasis in Europe, North America, New Zealand and Australia.

One of the dilemmas in developing a new crop is that extraction facilities for extracting the ultimate active ingredient (which may be relatively small in size in the early stages of its development) are not readily available. For this reason, Kings recently acquired a solvent extraction facility in Lincolnshire, which is capable of producing pharmaceutical grade products from as little as 10 kgs in size, up to thousands of tonnes.

The types of crops that Kings are involved in include High Erucic Acid Rapeseed for the production of erucamide, a slip agent used in polythene bags; along with crambe, another source of High Erucic Acid. Kings are also well known for the production of Borage for the supply of GLA, and have also pioneered work on the development of saponins from Quinoa for pharmaceutical uses. Other crops include Camelina and Calendula along with many other cosmetic and pharmaceutical crops which are often grown under confidentiality agreements for clients.

2. Identity Preserved Production

It is perhaps useful to define what identity preserved (IP) production really means. IP production involves a fully traceable system detailing the history of the crop, from the sowing of the seed right through to the resulting extracted product. Within this, it is important that the IP scheme is documented, and ultimately audited, in order to provide confidence to the customer. Documented production systems, open to audit and scrutiny to the end user can have a significant effect on the end product's characteristics.

IP production will become more and more important, particularly following the many recent food scares, which have come to the attention of the media. BSE, the use of GMO's, E Coli and recently Dioxin's have all made the ultimate consumer far more aware of what he is eating. Customers wish to express a choice in what they, and their families, consume and, irrespective of whether their worries are scientifically justified, the customer's perception can have a significant effect on a company's profits.

For pharmaceutical markets an IP system is essential, as the R & D investment in a project can be very significant. Plants are a natural product and cannot be as easily controlled as the manufacture of nuts and bolts in a factory for example. Things can go wrong and the whole point of having an IP system is to try and control the uncontrollable.

The recent interest in genetically modified crops not only puts an enormous emphasis on having an IP system when growing GMO's, but also now customers need to be guaranteed that their non-GMO crops are free from this new technology.

It is interesting to note that 10% - 15% of Europe's consumption of medicinal and aromatic plants is from cultivated species (Svoboda et al 1999). Collections from the wild therefore, still account for a significant portion of the market (over 85%) and hence the need to try and control, to as great a degree as possible, the basic raw material that pharmaceutical, cosmetic and food companies want to use.

This variability of product can have a significant effect on ultimate performance. A good example of this is the large number of products available in chemist and health food shops of Hypericum Perforatum. Manufacturers have found to their cost that all Hypericum Perforatum is not the same and the amount of hypericin and hyperforin within in different lots of produce can vary tremendously.

Consistent quality can only be assured if the starting materials are defined in a rigorous and detailed manner. This includes the botanical identification, the geographical source and the conditions of production.

Starting with the seed originally sown to produce a crop, there are clearly many dilemmas. Plant breeders will not dedicate significant amounts of money into a crop which may only ultimately become 50 – 100 ha's in size and, therefore, landrace strains of a species will often need to be used. Variability in natural species can be significant and it is, therefore, essential to analyse the seed or plant before planting to ensure that it contains the target active ingredients. It is also important to understand how the plant performs in terms of when to harvest, what to harvest and how to maximise the target active that is being sought.

Clinical trials carried out on St John's Wort demonstrated significant differences in the performance of this herb. The presence or absence of hyperforin, one of the target active ingredients, resulted in the trial either being a success or a failure. Clearly a buyer does not wish to buy material which subsequently fails to perform in the consumers' hands. It is essential therefore, that the material used for trials must be grown from the same stock which will ultimately be used to provide the final marketed product.

The area of geographical production can also have a significant effect on the resulting end product. The percentage bilobalide extracted from Ginkgo biloba has been shown to vary tremendously depending upon where it is grown. Within this, the season can also have an effect and just because the production of a crop in a certain country has done well in one year, does not automatically mean it will perform the same in the following season. The need therefore, to produce crops in different locations becomes quite evident.

The timing of harvest can also significantly affect the level of active ingredients, but if the history of a raw material is not known, (if it has just been bought on the open market for example) then significant differences can exist between different lots.

One important area that is often overlooked is in the various contaminants that can occur in plant extracts. Heavy metals, micro-organisms, the use of fumigants and pesticide residues are all important quality characteristics. Although all of these can be tested in a product, if the crop has not been produced on an IP basis the seller will not know where a problem has arisen and whole batches of raw material may be rejected if they fail to conform to the buyers specifications. Tests carried out by the California Department of Health Services (Busse 1999) have shown severe contamination in some Chinese herbs, some 1,000 times over recommended maximum limits.

Microbial contamination, which can be influenced by the method of harvesting and the amount of soil picked up by the harvester can also have significant negative effects.

Contrary to popular belief IP production systems do not stop once the crop has been harvested. The haulage of the crop to the processing facilities also has to be monitored, and the way in which the plant material is extracted can all have a bearing on the resulting characteristics. The type of solvent used and the previous crop processed all need to be taken into account. If the previous crop possesses some undesirable characteristic, such as a strong colour or taint, then without thorough cleaning these contaminants can pass though to the next batch that is processed. It is quite easy to understand why audited quality systems such as Good Agricultural Practise, Good Manufacturing Practise and Good Laboratory Practise are all essential precursors to the supply of a quality product.

3. Commercial Development of Novel Crops

The commercial development of a successful new crop can often be a long process. Key questions have to asked throughout the evaluation process including whether the end product will have a quality that is stable, is able to be replicated and offer 100% confidence to the customer. A detailed agronomic programme has to be implemented, along with a review of the geographically most suitable production areas in order to offer both competitive and guaranteed sources of raw material.

The most successful new crop developments are often those that have been market- rather than product-orientated. A market-orientated development programme will first identify a customer's need. For example, a company approached Kings to

develop Saponins for a specific pharmaceutical use and subsequently Kings evaluated a wide range of different species to identify plant types that could produce the target saponins in the most economic fashion. Having developed an idea, it is important to protect the intellectual property that has been created and this can be done by means of patents as well as plant breeders' rights.

An example of a product-orientated production could be Evening Primrose. If the price of Evening Primrose is high, growers in China will respond to the demand resulting in massive over-production and a consequent fall in the price of EP oil. Similar examples include Echinacea in Australia, where many growers saw the market for Echinacea getting larger, jumped on the bandwagon and successfully collapsed the market overnight. Understanding supply and demand can be a very painful lesson. Over producing 100 tonnes of a product does not increase the market by 100 tonnes, it simply depresses the price. Contrary to popular belief, manufacturers and customers do not want a product which is very price volatile. Far more important is a consistent product at a consistent price.

A typical commercial development process at King's includes the evaluation of trial material in plots. Once interesting species have been identified, these are taken up on a replicated trial basis, and at this stage, different methods of extraction methodology are looked into. Once on a limited field scale production, pilot extraction can then take place. Following further research and development work, commercial production can take place once a full agronomic programme has been established.

The aim of all this work is to produce a target active ingredient as competitively as possible for the customer. Considerations, such as geographical area of production, the various species that can be chosen and the variability of production are all-important issues.

Although many of the crops that Kings grow are not dependent on Area Aid from the EU, the effects of the CAP need to be taken into account. With Agenda 2000, a flat rate of aid is due to be paid to growers, irrespective of the crop they wish to grow. However, not all crops are eligible, and this can provide an economic barrier to entry. Camelina is a good example of this, which is a source of Alpha Linolenic Acid (ALA). Yielding the same as Spring Oilseed Rape, it needs to be priced at least £120/tonne more, in order to encourage growers to produce it. Clearly this can result in a crop being uncompetitive despite it offering useful advantages to the end user.

If a customer is to be encouraged to support a new crop, he must be certain that he can obtain the raw materials year in year out. A Manufacturing Director of a large factory is not going to be too impressed if he is told that only half of what he has ordered is available due to a poor harvest. Production in different geographical areas and over-yearing products can be used to reduce the risk of this happening but clearly there is a cost associated with this. The percentage active ingredient in a plant can also vary season on season but products can be standardised using blending methods if the history of the crop is well documented.

4. Conclusion

In summary, it is essential to understand the market in developing a new crop. For every success story, there will be many failures, but an understanding of the customer's requirements will help to reduce this tremendously. Having identified an opportunity, Identity Preservation is vital. Customers are becoming far more aware of the difference between cost and value. The cost of raw materials is clearly the largest part in many production processes. Companies which lack their own contract production facilities and have to buy on the open market, can only offer one thing and that is price. Identity Preservation offers the customer quality assurance, consistency, continuity, repeatability and most important of all – peace of mind.

5. References

Busse, W (1999)	APV Seminar "Quality of Herbal Products", Darmstadt, Germany
Svoboda, K P, Hampson, J B, Galambosi, B	Aromatic and Medicinal Plants – Sources of Natural Products